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African American Women

PRINCIPAL INVESTIGATOR: Chanita Hughes, Ph.D.

CONTRACTING ORGANIZATION: Georgetown University Medical Center  
Washington, DC 20007

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## Table of Contents

Cover.....	1
SF 298 .....	2
Table of Contents .....	3
Introduction.....	4
Body .....	4
Key Research Accomplishments .....	8
Reportable Outcomes.....	9
Conclusions.....	10
References.....	11
Appendix.....	12

## A. INTRODUCTION

Five to 10% of all breast cancer cases have been attributed to two breast-ovarian cancer susceptibility genes called BRCA1 and BRCA2. Genetic testing for BRCA1/2 mutations is now available through clinical research programs using standard counseling protocols. The goal of pre-test counseling is to facilitate informed decision making about whether to be tested and to prepare participants for possible outcomes. The goal of post-test counseling is to provide information about risk status, recommendations for surveillance, and options for prevention. However, previous research on genetic counseling suggests that African American and Caucasian women differ in their attitudes and responses to genetic education and counseling. Increasingly, the cultural beliefs and values of participants are being recognized as important factors in genetic counseling. However, despite broad recommendations to increase the cultural sensitivity of breast cancer risk counseling, such programs have not been developed or evaluated. Therefore, the purpose of this study is to develop a Culturally Tailored Genetic (CTGC) protocol for African American women and evaluate its impact compared with Standard Genetic Counseling (SGC) in a randomized clinical trial. This research is linked with Dr. Hughes' Career Development Award and has the following primary technical objectives:

**(1) To evaluate the relative impact of CTGC vs. SGC on decision-making and satisfaction about BRCA1/2 testing.** Compared to SGC, CTGC will lead to higher rates of test acceptance and satisfaction with testing decisions. These effects will be mediated by increases in perceived benefits and decreases in perceived limitations and risks of genetic testing.

**(2) To evaluate the impact of CTGC vs. SGC on quality of life and health behaviors following BRCA1/2 testing.** Compared to SGC, CTGC will lead to larger decreases in general and cancer-specific distress, greater increases in adherence to cancer screening guidelines, and lower rates of prophylactic surgery. Reductions in psychological distress will be mediated by increased use of spiritual coping strategies.

### Secondary Aim

**To identify African American women who are most and least likely to benefit from CTGC vs. SGC.** We predict that the relative benefits of CTGC will be greatest for women with greater endorsement of African American cultural values and those identified as BRCA1/2 carriers.

## B. BODY

The research was initiated in September 2000. The first year of the study focused on (1) developing intervention materials, (2) creating data management systems, and (3) hiring study personnel. This project is linked with Dr. Hughes' Career Development Award (CDA) and activities regarding professional development are provided in section 4.

We are requesting a change of grantee institution because Dr. Hughes has moved to the University of Pennsylvania Medical Center. This report reflects work completed during months 1-8 of the project while Dr. Hughes was at the Georgetown University Medical Center. During months 9-12, Dr. Hughes was preparing to move to the University of Pennsylvania Medical

Center and activities completed during this time frame are also included in section 5 of this report.

(1) Intervention Materials. Eligible subjects for this study include African American women who have a personal and/or family history of breast or ovarian cancer. During the first year of the study, we developed genetic education materials specifically for African American women. This material is an educational booklet that was designed to provide information about breast cancer among African American women, inherited breast cancer susceptibility among individuals of African ancestry, and information about breast cancer syndromes (i.e., sporadic, familial, and hereditary disease). Information about BRCA1 and BRCA2 cancer susceptibility genes and the process of genetic testing is also provided in the education booklet. Although this information will be covered extensively during the in-person SGC and CTGC counseling sessions, we believe that provision of this information in written format would supplement the education and counseling that is provided as part of both protocols. Further, prior studies have shown that African American women are less knowledgeable about breast cancer genetics (Hughes et al., 1997; Donovan et al., 1999) and provision of written information along with counseling is likely to increase comprehension of concepts related to hereditary breast cancer and genetic testing. Also, it is standard practice to provide written educational materials along with genetic education and counseling; thus, inclusion of educational materials that are designed to address breast cancer issues among African American women will increase the validity and generalizability of the counseling protocols that will be delivered as part of this study. A copy of the educational booklet is provided the Appendix.

(2) Data Management Systems. During the first eight months of the study, a Window's based data management system was created to store study data and track research participants. Specifically, Microsoft Access relational databases were created to store research data and these databases were designed to maintain information regarding subject contact information, questionnaire data, and genetic test result information. All subject information (i.e., questionnaire data, genetic test results) is entered using a unique identification number. Subject contact information (i.e., name, telephone number, address) is maintained in a separate database. To further protect the participant's confidentiality, genetic test results are stored in a separate table that is not linked with subject identifying information. Specifically, test result information is tracked with a randomly generated key field that is controlled by the principal investigator. We also integrated security procedures within the data management system to further protect the confidentiality of study participants. These security procedures include (a) secure data storage, (b) password protection, and (c) use of confidential identification numbers rather than subject's names.

(3) Study Personnel. We hired a Master's level Genetic Counselor to deliver the study protocols. To ensure that the process and format of our counseling protocols are consistent with those used in standard genetic counseling protocols, the genetic counselor completed training on cancer risk counseling and breast cancer genetics through the Cancer Risk Assessment and Evaluation program at the Georgetown University Medical Center. The genetic counselor also completed training on cultural and ethnic issues in decision-making about cancer prevention and control strategies. Dr. Hughes provided this training during months 1-8 of the project.

(4) Career Development Activities. Because this project is linked with Dr. Hughes' career development award, a summary of the professional development activities that were completed during the last year is included in this report. During the past year, Dr. Hughes was an active member of the cancer genetics research program at the Georgetown University Medical Center and a listing of the manuscripts published during the past year is provided in section D. Although these manuscripts are not based on data derived from this project, Dr. Hughes' contributions on these manuscripts are directly related to her professional development and her involvement with the preparation of these manuscripts (i.e., theoretical and methodological conceptualization, statistical analysis) has provided valuable experiences that are directly transferable to this project. For example, Dr. Hughes is co-author on a manuscript that evaluated decision-making about genetic testing for inherited breast cancer risk (see Schwarz, Hughes et al., 2000) and is also a co-author on a manuscript that evaluated the impact of BRCA1 and BRCA2 test results on health behaviors (see Lerman, Hughes et al., 2000). These manuscripts address the two primary outcomes of this study and the experiences learned through working on these publications will facilitate Dr. Hughes' ability to generate scholarly publications based on the data from this project.

In addition to contributing to the manuscripts described below in section D, Dr. Hughes also completed analyses of data related to cultural beliefs and values among African American women who had a personal and family history of breast cancer and/or ovarian cancer. Participants in this analysis were 28 high-risk African American who completed measures of cultural beliefs and values as part of their participation in the Cancer Assessment and Risk Evaluation program at the Georgetown University Medical Center. First, means and standard deviations were generated to characterize participants in terms of their cultural beliefs and values and the average level of communalism was 113.9 (S.D.=11.9). In terms of religious coping style, participants reported the greatest levels of collaborative religious coping. The mean level of collaborative religious coping was 24.5 (S.D.=5.5) while the mean levels of self-directing and deferring religious coping were 11.0 (S.D.=5.3) and 19.5 (S.D.=6.9), respectively. The mean levels of temporal orientation were consistent with a flexible time perspective. For example, the mean levels of past (Mean=45.6, S.D.=9.7) and future (Mean=41.8, S.D.=8.8) temporal orientation were greater than the mean levels of present (Mean=31.4, S.D.=7.6). Because we were interested in the level of endorsement for the specific components of each cultural belief and value, we also generated item frequencies for each cultural factor. For these analyses, items were re-coded to reflect the level of endorsement for each factor in terms of the percentage of respondents who agreed or strongly agreed with each item. A summary of these results is provided below for each cultural factor.

**Communalism.** The most strongly endorsed component of communalism was interest in advice from older family members. Specifically, 93% of respondents reported that it was mostly or completely true that they were always interested in what older relatives have to say because age leads to wisdom. Fictive kin relationships were also highly endorsed among study participants and 92% of respondents reported that it was mostly or completely true that there are close friends who are considered family and 71% reported that it was mostly or completely true that it is not unusual to refer to friends using relationship terms (i.e., aunt, uncle). Familial responsibilities and maintaining the quality of relationships with relatives was also strongly endorsed among respondents. More than 80% of respondents reported that it was mostly or completely true that

they were constantly aware of their responsibility to family members and friends, individuals have an obligation to cooperate with family and friends, and sacrifices are made for family members while only 39% of respondents reported that it was mostly or completely true that their first responsibility is to themselves rather than family members. Relatives were also viewed as an important source of social support; 82% of respondents reported that it was mostly or completely true that family members turn to one another during a crisis and 71% reported that it was mostly or completely true that older family members are relied on for advice or guidance. Further, while only 36% of respondents reported that it was mostly or completely true that family group membership gives them a sense of personal identity, 60% of respondents endorsed the belief that people should not view themselves as independent of family or friends.

**Religious Coping Style.** In terms of religious coping, collaborative coping strategies were the most strongly endorsed and more than 80% of respondents either agreed or agreed strongly with items that assessed utilization of collaborative religious coping strategies. For example, more than 80% of respondents endorsed coping strategies in which they worked together with God to decide what a problem means and to develop solutions to difficult situations. The importance of collaborative coping strategies was also reflected in the lower levels of endorsement for items that assessed utilization of self-directed or deferring religious coping strategies. For example, items that assessed utilization of deferring religious coping strategies were endorsed by 39% to 57% of respondents and only 4% of respondents reported that they agreed or agreed strongly that they acted to solve problems without God's help. In addition, only 11% of respondents reported that they agreed or agreed strongly that they try to cope with difficult situations without God's help.

**Temporal Orientation.** In terms of temporal orientation dimensions, the most strongly endorsed belief regarding past temporal orientation was related to the emotional impact of thinking about past events and 86% of respondents reported that thinking about the past makes them very emotional. In terms of future temporal orientation, the most strongly endorsed belief was related to sticking to a plan in order to get ahead and the least endorsed belief was related to implementing a plan to get things done. Specifically, 89% of respondents endorsed the belief that they keep working at a difficult, boring task if it will help them to get ahead while only 24% of respondents endorsed the belief that when they want to get things done, they make detailed plans and think of how to complete each step.

In addition to being actively involved in the cancer genetics research program at the Georgetown University Medical Center, Dr. Hughes was invited to join several national committees related to cancer genetics. These include the Behavioral Science Working Group and the Education and Communications Committees of the Cancer Genetics Network (CGN). The CGN was established by the National Cancer Institute (NCI) to develop the infrastructure needed to conduct systematic and organized empirical research on inherited cancer susceptibility. The mission of the Behavioral Science Working Group is to facilitate the development and implementation of research concepts on the social and behavioral science of cancer genetics research and to provide input and consultation on behavioral science and counseling issues relevant to the CGN. The mission of the Education and Communications Committee is to develop research concepts within the CGN to advance understanding about issues regarding provision of education and counseling and to develop and evaluate methods and systems for

communicating genetic risk information. Dr. Hughes will continue to be actively involved in the Behavioral Science Working Group at the University of Pennsylvania Medical Center, which is one of the eight academic medical centers funded by the NCI as a CGN center.

(5) Activities Completed at the University of Pennsylvania Medical Center. As described above, Dr. Hughes has moved to the University of Pennsylvania Medical Center and months 9-12 of the project were spent preparing for the move. In anticipation of receiving approval of the request to transfer the grant to Dr. Hughes' new institution, this time has also been spent completing activities to facilitate conducting the project at the University of Pennsylvania Medical Center. These activities included transferring the data management system described above to the University of Pennsylvania Medical Center. We expect to have this action completed by mid-October and once this transfer has been completed, the data management system will be stored on a secure Window's NT server that is located in the Transdisciplinary Tobacco Research Center and Community and Minority Cancer Control program at 3535 Market Street, Suite 4100, Philadelphia, PA. We have also initiated actions to hire study personnel. We have identified a candidate for the research assistant position and we began recruiting a new genetic counselor to deliver the interventions at the University of Pennsylvania Medical Center. This candidate accepted another position and we are now in the process of recruiting another genetic counselor and expect to also have this action completed by mid-October. We have also spent months 9-12 of the project revising study materials and establishing systems for subject recruitment through the University of Pennsylvania Cancer Center Network and community organizations such as the Greater Philadelphia Chapter of the National Black Leadership Initiative.

### C. KEY RESEARCH ACCOMPLISHMENTS

The first year of the study focused on focused on developing the intervention materials, creating data management systems, and hiring study personnel. The key research accomplishments achieved during the past year include creating educational materials about hereditary cancer and genetic testing specifically for African American women and analyzing data related to cultural beliefs and values among high-risk African American women. These activities are significant for several reasons. First, although published reports are now available to further describe hereditary breast cancer among African Americans (Gao et al., 1997; Gao et al., 2000; Mefford et al., 1998), to our knowledge, this information has not yet been incorporated into standard genetic counseling protocols in a written format. We have assembled this data into a written educational booklet that is designed to supplement the counseling protocols that will be delivered in this project. In addition to developing this educational tool, we have also completed analysis of data related to cultural beliefs and values among high-risk African American women. Through this analysis, we have identified cultural beliefs and values that are most important to African American women. For example, more than 80% of respondents reported that advice from family members and maintaining the quality of relationships with family members are key values. These findings are consistent with our previous research on attitudes about genetic testing which found that African American women are more likely to report concerns about the impact of genetic testing on their family members (Hughes et al., 1997) and suggests that pre-test counseling should focus on both individual preferences and considerations of the impact of testing on family members. Also, the mean levels of temporal orientation and the pattern of

responses related to the specific temporal dimensions suggest that past events and future outcomes are likely to be the most valued by high-risk African American women. These findings have important implications for how past experiences with breast and ovarian cancer is discussed during education and counseling as well as how genetic testing may be conceptualized in terms of achieving future health outcomes. Consistent with our previous research (Hughes et al., 1996), we also found that African American women were most likely to endorse collaborative religious coping strategies. More than 80% of respondents reported that they worked with God to understand problems and develop solutions. These findings suggest that collaborative coping strategies may be used by African American women in making decisions about whether or not to have genetic testing as well as to cope with the outcome of testing.

#### D. REPORTABLE OUTCOMES

##### Manuscripts Published as Part of Career Development Activities

Schwartz M, Hughes C, Roth J, Main D, Peshkin BN, Isaacs C, Kavanagh C, Lerman C. Spiritual faith and genetic testing decisions among high risk breast cancer probands. *Cancer Epidemiology, Biomarkers and Prevention*, 2000; 9(4):381-386.

Lerman, C, Hughes, C, Croyle RT, Main D, Durham C, Snyder C, Bonney A, Lynch JF, Narod SA, Lynch HT. Prophylactic surgery decisions among BRCA1/2 families. *Preventive Medicine*, 2000; 31(1):75-80.

Tercyak K, Lerman C, Hughes C, Main D, Snyder C, Lynch J, Lynch H. Parental communication of genetic test results. *Patient Education and Counseling*, 2001; 213-24.

Hughes C, Lerman C, Schwartz M, Peshkin BN, Wenzel L, Narod S, Corio C, Tercyak KP, Hanna D, Isaacs C, Main D. All in the Family: An evaluation of the process and content of sister's communication about BRCA1 and BRCA2 genetic test results. *American Journal of Medical Genetics*, in press.

Tercyak K, Lerman C, Peshkin BN, Hughes C, Main D, Isaacs C, Schwartz MD. Effects of coping style and BRCA1/2 test result on anxiety among women participating in genetic counseling and testing for breast/ovarian cancer risk. *Health Psychology*, in press.

Schwartz MD, Peshkin B, Hughes C, Main D, Isaacs C, Lerman C. The Impact of BRCA1/BRCA2 Mutation Testing on Psychological Distress in a Clinic-Based Sample. *Journal of Clinical Oncology*, in press.

Cella D, Hughes C, Schwartz M, Wenzel L, Marcus A, Peshkin B, Lerman C. The Multi-Dimensional Impact of Cancer Risk Assessment (MICRA) Instrument. *Health Psychology*, under review.

Invited Presentations Delivered by Dr. Hughes

"Genetic Testing for BRCA1 and BRCA2 Mutations." Seventh Annual Research Centers in Minority Institutions, International Symposium on Health Disparities, San Juan, Puerto Rico

"Emerging Issues in Genetic Counseling and Testing for Inherited Cancer Risk." The 14<sup>th</sup> International Symposium for the Foundation for Promotion of Cancer Research, Pain Control, Palliative Medicine, and Psychooncology: Present Status and Future Direction, Tokyo, Japan

"Minority Issues in Genetic Counseling and Testing for Inherited Cancer Risk." The Cancer Family: At the Intersection of Science and Society Conference, Charlottesville, VA

"Sociocultural Considerations in Genetic Counseling and Testing for Inherited Cancer Risk." Fred Hutchinson Cancer Research Center, Seattle, WA

**E. CONCLUSIONS**

During the first year of the study, our activities focused on developing intervention materials, creating a data management system for our research data, and hiring study personnel. Although there has been reduced productivity in terms of completing the final CTGC protocol due to having to stop work on the project in order to prepare for Dr. Hughes' move to the University of Pennsylvania Medical Center, we have completed analysis of data regarding cultural beliefs and values and the results from this analysis will be used in developing the final version of the CTGC protocol at the University of Pennsylvania Medical Center. Dr. Hughes is also in the process of submitting a manuscript that is based on these data. Previous research designed to evaluate the impact of cultural factors on cancer prevention and control behaviors has focused on folk health beliefs among African American women (Lannin et al., 1998) or has inferred cultural beliefs and values from ethnic differences in beliefs and attitudes (Hughes et al., 1997). While ethnic differences and folk beliefs may reflect underlying cultural beliefs or values, folk beliefs may have limited generalizability and ethnicity is only an approximation of cultural factors. Support through this project allowed Dr. Hughes to complete these analyses and the data obtained through this effort will be used to develop the final version of the CTGC protocol and will also make an important contribution to the scientific literature by furthering our understanding of the prevalence of cultural beliefs and values among African Americans.

Although there has been an interruption of work on the study due to Dr. Hughes' move to the University of Pennsylvania Medical Center, we have tried to minimize this interruption by completing activities that will enable us to begin work on the study at the new institution after approval for this transfer has been obtained. Specifically, in anticipation of receiving approval for this transfer, months 9-12 of this year of the project were spent preparing for Dr. Hughes' move to the University of Pennsylvania Medical Center and completing activities that will facilitate conducting the study at her new institution once approval is granted. As described above, we expect to have these actions completed by mid-October. As a result of completing these actions, we will be able to complete the project within the original time frame for the study and our plans are to complete development of the CTGC protocol, initiate subject recruitment,

and conduct the education and counseling sessions at the University of Pennsylvania during the remaining project period.

## F. REFERENCES

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Gao Q, Tomlinson G, Das S, et al. Prevalence of BRCA1 and BRCA2 mutations among clinic-based African American families with breast cancer. *Hum Genet.* 2000;107:186-91.

Hughes C, Lerman C, Lustbader E. Ethnic differences in risk perception among women at increased risk for breast cancer. *Breast Cancer Research and Treatment.* 1996; 40:25-35.

Hughes C, Gomez-Caminero A, Benkendorf J, et al. Ethnic differences in knowledge and attitudes about BRCA1 testing in women at increased risk. *Patient Education and Counseling.* 1997; 32:51-62.

Lannin DR, Mathews HF, Mitchell J, et al. Influence of socioeconomic and cultural factors on racial differences in late-stage presentation of breast cancer. *JAMA.* 1998;279:1801-7.

Mefford HC, Baumbach L, Panguluri RC, et al. Evidence for a BRCA1 founder mutation in families of West African ancestry. *Am J Hum Genet.* 1999;65:575-8.

**APPENDIX**

***WITH OUR VOICES***  
**EDUCATIONAL MATERIAL**

*An Information Guide on Cancer Genetics for African American Women*

*With Our Voices*  
A Cancer Education Program for African American Women

## Overview

This booklet was designed for women with a personal or family history of breast or ovarian cancer who are interested in learning more about hereditary breast cancer. A great deal of information was discussed with you during your genetic counseling session. We are providing this booklet to review this information. Specifically, this booklet reviews factors that might increase a woman's breast and ovarian cancer risk, the process of genetic testing, possible outcomes of testing, and recommendations for screening and prevention. This booklet also reviews breast cancer issues that are particularly of concern for African American women.

In addition, the words presented in *italicized* text are defined in the section at the back of the booklet.

If you think of additional questions after reading this booklet please contact your genetic counselor.

## Table of Contents

About The "With Our Voices" Research Program.....	2
Breast Cancer in Black Women.....	3
Breast Cancer Risk Factors.....	4
Ovarian Cancer Risk Factors.....	6
Genetic Risk for Breast and Ovarian Cancer.....	7
BRCA1 and BRCA2 Cancer Susceptibility Genes.....	9
Inheritance of Cancer Susceptibility.....	10
The Genetic Testing Process.....	11
Cancer risks associated with BRCA1 and BRCA2 mutations.....	14
Cancer Screening.....	16
Breast and Ovarian Cancer Prevention.....	19
Genetic Testing Pros and Cons.....	21
Resources.....	23
Glossary.....	24

## **The “With Our Voices” Research Program**

With Our Voices is a research program for African American women who have a personal or family history of breast or ovarian cancer. This project was designed to take into consideration the unique aspects of the experiences that African American women with breast cancer may have in order to provide you with information about some of the things that may be important as you consider genetic testing. Through the program each participant meets with a genetic counselor to discuss: your family history of cancer; how cancer may be passed down in families; and recommendations for *screening* and prevention.

One of the goals of this research project is to determine the best methods of providing education and counseling about genetic testing for *inherited* breast and ovarian cancer risk to African American women. Therefore, women who participate in this project are randomly assigned to one of two different genetic counseling approaches.

You will also be asked to complete telephone interviews and questionnaires both before and after your counseling session. This information will help us learn more about how women make decisions about genetic testing and the impact of the decision on their lives. Our knowledge of these factors in African

Americans is currently limited. Therefore, your participation in this project is of particular value as we strive to increase our understanding of these issues so that more effective programs can be developed for African American women and their families.

## **Breast Cancer in Black Women**

Breast cancer is a major health issue for all women as 1 in 8 women will develop breast cancer in her lifetime. There have been efforts to ease the burden of the disease through education, prevention, early detection, and treatment. Despite overall success of these efforts, the breast cancer epidemic continues to be particularly concerning for African American women. Although Black women are less likely to develop breast cancer overall, they have a higher likelihood of dying from this disease. This difference in cancer survival is not completely understood. However, possible factors which may contribute to lower survival among African American women include differences in risk factors, screening practices, and tumor characteristics. Black women are also consistently diagnosed with more advanced stage breast cancer. Overall, breast cancer treatment is more successful when the cancer is diagnosed at an early stage. Therefore, late stage diagnosis of breast cancer may be another factor in the lower survival rates among Black women. Several studies are being conducted to identify factors that contribute to lower survival rates and quality of life following breast cancer among Black women.

Breast cancer in African American women has also been found to share characteristics with breast cancer

in women with *hereditary* breast cancer. For instance, *hereditary* breast cancers are often diagnosed in women at an earlier age (less than 50 years) than is typically seen in the general population. Similarly, it has been observed that African American women are also more likely to be diagnosed with breast cancer at a young age (30-49). There are also similarities between the *pathology* of breast tumors in Black women and women with hereditary breast cancer. Tumors in young African American women as well as women with hereditary breast cancer are more likely to be poorly differentiated and estrogen receptor negative. These similarities suggest a genetic contribution to breast cancer in Black women. However, we have much to learn about this possibility.

## Breast Cancer Risk Factors

Breast cancer is a common disease, and thousands of women are diagnosed with breast cancer each year in the United States. The specific causes of breast cancer are still unknown. However, it is clear that breast cancer is not caused by bumping, bruising, or touching the breast. Although we know about factors that may increase a woman's risk of developing breast cancer, many women who have known risk factors do not get breast cancer. Several factors that have been found to increase a woman's chance of developing breast cancer are described below.

**Age:** The risk of breast cancer increases as a woman gets older. Most breast cancers occur in women over the age of 50; the risk is especially high for women over age 60. Breast cancer is uncommon in women under the age of 35. However, women with an inherited susceptibility to breast cancer face an increased risk of developing this cancer in their 30s and 40s.

**Family History:** The risk of getting breast cancer is higher among women who have one or more close relatives with the disease. More specifically, a woman who has a mother, sister, or daughter who's been diagnosed with breast cancer has a 2 to 3 times higher risk of developing the disease. In addition, the

woman's risk may further increase if her relative's cancer were diagnosed before menopause or if breast cancer was diagnosed in both breasts. Although many women with breast cancer have a close relative with the disease, only about 5-10% of women have a *hereditary* form of breast cancer. A family tree constructed by a genetic counselor is a useful tool to help determine whether an individual's family history is suggestive of an *inherited* pattern of cancer.

**Previous Cancer:** Women who have had breast cancer before face an increased risk of getting breast cancer again. For example, a woman can still develop breast cancer in her opposite breast after having a mastectomy. As many as 10% to 15% percent of women treated for breast cancer (or *ductal carcinoma in-situ*) get a second primary (new) breast cancer.

**Biopsy History:** Women who have had breast biopsies that show certain *benign* changes in breast tissues, such as *atypical hyperplasia* or *lobular carcinoma in situ*, have an increased risk of breast cancer. This risk is even higher if a woman has a close relative with breast cancer.

**Reproductive Factors:** There are risk factors for breast cancer that are related to a woman's natural hormones. Having a first period at an early age (before 12), having a late menopause (after 55), never

having children, or giving birth to a first child after age 30, all can increase a woman's risk for breast cancer. These hormonal factors are thought to contribute to the lower incidence of breast cancer in Black women because, on average, Black women experience menopause at a younger age than White women and are younger when they give birth to their first child. However, keep in mind that breast cancer can still develop among women who do not have any risk factors and Black women are at greater risk for developing breast cancer at younger ages.

**Hormone Use:** Long term use of birth control pills in women under age 25 may be associated with a slight increase in the risk of developing breast cancer at a young age. This data may be of particular importance for African American women since studies suggest that they begin birth control use at an earlier age than White women. Studies have also shown that long term hormone replacement therapy (HRT) increases breast cancer risk. It is also thought that the risk may be higher for combination HRT (*estrogen and progesterone*) versus *estrogen* alone.

**Other Factors:** Some aspects of a woman's lifestyle may affect her chances of developing breast cancer. For example, women who drink alcohol excessively have a slightly higher breast cancer risk. Therefore, women who drink should do so only in moderation.

Older women who are overweight seem to have a greater risk of breast cancer. In general, the link between diet and breast cancer risk is still unclear; however, reducing fat in the diet can reduce the risk of other diseases that are common among African Americans such as diabetes, hypertension and heart disease.

Bear in mind that the extent to which factors below may affect the risk of a woman with an inherited *predisposition* to breast cancer is largely unknown.

## Ovarian Cancer Risk Factors

About 1 in 57 women in the United States will develop ovarian cancer in her lifetime. Similar to breast cancer, the exact causes of ovarian cancer are not known. However, studies have shown that the following factors may increase the chance of developing the disease. Keep in mind that having one or more of the following risk factors does not mean that a woman is sure to develop ovarian cancer.

**Age:** As with many cancers, age is one of the most significant risk factors for ovarian cancer. Ovarian cancer is more common in women over age 60, but often occurs in women with a family history of the disease before or during their early 40s.

**Family history:** First degree relatives (mother, daughter, sister) of a woman who has had ovarian cancer are at increased risk of developing this type of cancer themselves. The likelihood is especially high if two or more first-degree relatives have had the disease. A family history of breast or colon cancer is also associated with an increased risk of developing ovarian cancer.

**Childbearing:** Women who have never had children are more likely to develop ovarian cancer than women who have had children. In fact, the more

children a woman has had, the less likely she is to develop ovarian cancer.

**Previous Cancers:** Women who have had breast or colon cancer may have a greater chance of developing ovarian cancer than women who have not had breast or colon cancer.

**Use of Talc (baby powder) in genital area:** Talc is in many personal hygiene products and some studies suggest that women who have used talc in the genital area for many years may be at increased risk for developing ovarian cancer.

**Fertility drugs:** Drugs that cause a woman to ovulate may slightly increase a woman's chance of developing ovarian cancer. Researchers are currently studying this possible association.

**Other Factors:** Ovarian cancer is more common in women from industrialized Western countries than in women in other parts of the world. Although, there is not a specific explanation for this, it is believed that it may be due to a diet high in meat and animal fat, which is characteristic of industrialized nations.

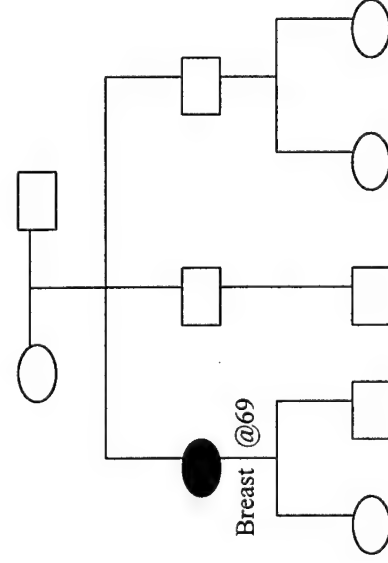
# Genetic Risk of Breast and Ovarian Cancer

Most breast and ovarian cancer cases are *sporadic* and only about 5 to 10 percent are *hereditary* in nature. A detailed description of the types of cancer that may be found in families (*sporadic*, *familial*, and *hereditary*) is provided below.

Sporadic (Low Risk) Families The majority of families in the general population fall into this category. Women who develop breast cancer later in life, usually after menopause, without a family history are described as having sporadic breast cancer. It is very unlikely that there is an inherited susceptibility to breast cancer in families with sporadic breast cancer.

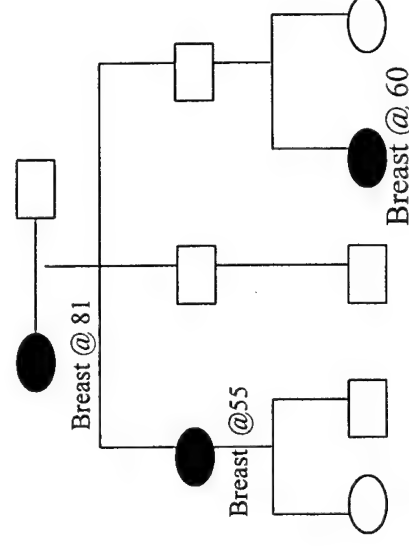
○ -Female    □ -Male    ● -Female with cancer

## Sporadic Breast Cancer



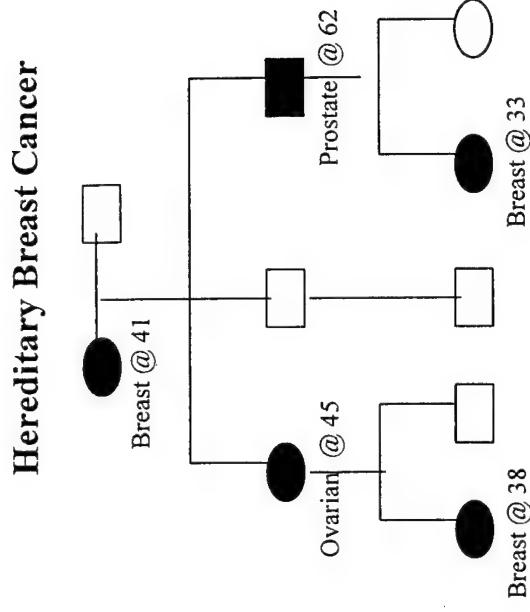
Familial (Moderate) Risk Families A clustering of late onset ( $>$  age 50) breast cancer in families is not uncommon. Given that one in eight women will develop breast cancer in her lifetime, it is not unusual to have several relatives in a family with breast cancer, especially in large families. In these families there is a less likely possibility that there is an inherited susceptibility to cancer in the family that is due to a single gene such as BRCA1 or BRCA2. However, the breast cancers in these types of families may be due to the interaction of more than one susceptibility gene and environmental factors.

## Familial Breast Cancer



### High-Risk (Hereditary) Families

Certain families are considered to have a “high risk” of carrying a *mutation* in a breast cancer *susceptibility* gene. When determining if a family is likely to have an inherited susceptibility to cancer due to mutations in BRCA1 or BRCA2 it is important to assess the family as a whole because these families have certain characteristics. These characteristics include breast cancer diagnosed before age 50 and ovarian cancers diagnosed at any age in many family members throughout several generations. However, ovarian cancer may not always be seen in families with hereditary breast cancer. Hereditary families may also have individuals who are diagnosed with more than one cancer, for instance some women may have both breast and ovarian cancer. The following family tree is an example of a high-risk family that is likely to have an inherited susceptibility to breast cancer. Keep in mind that although the pedigree below shows many of the characteristic features of hereditary breast and ovarian cancer, many families with hereditary breast and ovarian cancer may not have all of these features.



### **BRCA1 and BRCA2 Cancer Susceptibility Genes**

Scientists have discovered two genes called BRCA1 (BRCA1) and BRCA2 (BRCA2), that cause hereditary breast cancer. Individuals who have alterations (or mutations) in these genes may have a substantially increased risk of developing breast and ovarian cancer compared to individuals who do not have BRCA1 or BRCA2 gene alterations. While other breast cancer susceptibility genes may be discovered in the future, inherited alterations (called mutations) in the BRCA1 and BRCA2 genes account for the majority (80%) of hereditary breast and

ovarian cancers. BRCA1 and BRCA2 are thought to be "tumor suppressor" genes and when functioning properly, they help to prevent cancer from developing by making proteins that keep cells from growing abnormally. However, alterations in these genes can change their usual function. This change can increase a person's chance of developing breast, ovarian and some other cancers.

We are still learning about how common BRCA1 and BRCA2 gene mutations are in the general population, particularly among individuals whose ancestors come from Africa. However, it is thought that 1 of every 800 (around 0.1%) individuals in the general population carries a BRCA1 mutation in BRCA1, and the frequency of BRCA2 mutations appear to be more rare. Nonetheless, hundreds of BRCA1 and BRCA2 mutations have been identified among individuals from diverse ethnic backgrounds (i.e. African American, Eastern European). In addition, recent studies have found that BRCA1 and BRCA2 mutations are present among families of African and African American ancestry with a family history of breast cancer at rates that are comparable to European Americans.

Ethnic background may be an important factor in evaluating one's genetic risk of breast and ovarian cancer. For example, certain mutations called

"founder mutations" are mostly seen in specific populations who can trace their ancestry to a small group of individuals. Most Ashkenazi (Central or Eastern Europe) Jewish women who have hereditary breast cancer carry one of three BRCA1 or BRCA2 founder mutations. To date, one BRCA1 mutation has been identified of African ancestry which may be a founder mutation. However it appears that most mutations identified in African Americans are unique to families and few mutations have been found in unrelated families. Therefore, there are a large number of distinct and unique mutations among African Americans and many of these mutations have not been reported in Whites. More research is needed to understand African American founder mutations and to determine if others exist.

Currently, research in this area is increasing and there are very few studies have focused on BRCA1 and BRCA2 mutations in African Americans, thus our current knowledge is limited. However, your participation in this study will add to our understanding of hereditary cancer in the black population and which families are more likely to carry mutations in these genes. As we learn more about these mutations in African Americans, there will possibly be a more rapid and efficient means of genetic testing in the future. Also research to uncover how these genes specifically function to suppress

tumor growth will allow improved prevention, early detection, and treatment of cancer.

### **Inheritance of Cancer Susceptibility**

Most people understand the basic concept that we are a “shared” product of our parents because we have physical and personal qualities both our mother’s and our father’s. For instance, you may often be told that you look like your father or you may have asthma like your mother. A large part of this is explained biologically by our *genes* which are “instructions” for the human body. *Genes* control the growth, development and normal function of the body. When genes are working properly, our bodies are able to develop and function smoothly. However, an altered gene can result in deformity or the development of disease.

We all have two copies of every gene and we get one copy from each parent. Therefore, the BRCA1 and BRCA2 genes also come in pairs and everyone (both men and women) has two copies of each gene. An alteration or change in one copy of a gene pair can affect how the body functions even though the other copy of that gene may not be altered. In this situation, the altered gene tends to dominate over the working gene, which impairs the function of the gene. BRCA1 or BRCA2 gene alterations work in this way and if

one copy of the gene pair is altered a person may be at increased risk for developing certain types of cancers. In addition to BRCA1 and BRCA2, most other cancer susceptibility gene alterations are dominant.

Dominant gene alterations are inherited in a specific manner. The diagram below depicts the different ways that an individual can inherit a cancer gene alteration from their parent.

## Autosomal Dominant Inheritance

“A” stands for an altered copy of a cancer gene  
 “a” stands for functioning copy of cancer gene

♂ (Aa) Father has altered copy of cancer gene  
 ♀ (Aa) Mother has altered copy of cancer gene

♀ <b>Aa</b> Inherits a copy of altered cancer gene	♂ <b>aa</b> Inherits only functioning copies of cancer gene
♂ <b>Aa</b> Inherits a copy of altered cancer gene	♀ <b>aa</b> Inherits only functioning copy of cancer gene

As this diagram shows, an individual with a BRCA1 or BRCA2 gene alteration has a 2 in 4 or 50% chance of passing down that alteration to his or her children. This happens because eggs and sperm each carry only one copy of each gene pair. Thus, each child of a

parent with an altered gene has a 50% chance of inheriting the altered gene and a 50% chance of inheriting the normal functioning gene. The risk is not affected by the sex of the child or the affected parent, or by the child’s birth order. The risk also cannot be predicted based on how much a child may resemble one or the other parent in terms of physical characteristics such as eye color, height and hair color.

## The Genetic Testing Process

A genetic test for cancer *susceptibility* is different from most other medical test because it does not provide a specific diagnosis. Rather it tells a person whether they have *inherited* an increased possibility of developing cancer. A genetic test for cancer is also not associated with physical risks, but may involve how a person and their family members feel about the cancer in their family. For this reason, before testing and when test results are given, it is important to fully discuss the test and its implications with a genetic counselor.

If you decide to be tested, a small sample of blood will be drawn from a vein in your arm. Genetic material (called DNA) in your blood will be analyzed in a laboratory to detect changes (called mutations) in

your BRCA1 and BRCA2 gene. If you are the first one in your family to undergo testing, the type of genetic analysis that will be performed on your blood sample is called *sequencing*. Sequencing your BRCA1 and BRCA2 gene is similar to looking for a single spelling mistake in a several thousand page book. This is a very difficult task that may take several weeks. Therefore, results from this testing usually takes about 4-6 weeks to obtain.

It is important to mention that the first person to be tested in the family should be an individual who was diagnosed with breast cancer at a young age or with ovarian cancer. Testing is usually offered to a family member affected with cancer first because if there is a mutation in the family, there is a greater chance that a person with cancer will have inherited the mutation. Having an affected family member tested first also is more informative for the family. For instance, if a mutation is found in a relative with cancer then other family members can be tested for the specific mutation. On the other hand, if a relative who has not had cancer tests negative, there may still be a mutation in the family that this person did not inherit. For this reason we recommend that women who have been diagnosed with breast or ovarian cancer be tested first in families.

As previously mentioned, if a BRCA1 or BRCA2 mutation has been previously found in your family, a mutation specific test may be ordered. This test examines only a small portion of the DNA, in which the mutation in your family has been previously found. A mutation specific test is similar to looking for a single spelling mistake in a paragraph rather than in an entire book. Therefore, results from this type of analysis are usually available in a shorter period of time.

*There are several possible results from genetic testing that you may receive:*

You may receive a positive test result:

A positive test result means that a mutation known to increase the risk of breast and ovarian cancer was identified in your BRCA1 or BRCA2 gene. If you receive a positive test result, your relatives can be tested for the mutation found in you through this research program.

You may receive a negative test result:

A negative test result means that no mutations responsible for hereditary cancer risk were found. A negative test result is interpreted based on whether there is a known mutation in BRCA1 or BRCA2 in your family.

If you receive a negative test result and are the first person in your family to be tested, your result is considered inconclusive. This is because although a mutation was not found in your BRCA1 and BRCA2 genes, an inherited predisposition to breast and/or ovarian cancer may still be present in your family. A possible explanation for your negative result is that the cancer in the family is associated with a mutation in a cancer gene that has not yet been discovered and for which testing is not available. A negative result could also mean that a BRCA1 or BRCA2 mutation is present in a portion of the genes that current testing procedures do not analyze. In such cases, cancer risk is based on family history.

If you test negative for a BRCA1 or BRCA2 mutation that has been found previously in your family then you are considered to be a "true negative". A true negative result means that you did not inherit the gene mutation that is responsible for the cancer in your family. Therefore, your risk for breast and ovarian cancer is considered to be that of the general population. It also means that you cannot pass on the familial mutation to your children.

You may learn that you have a BRCA1 and/or BRCA2 variant(s) of uncertain significance:

Your test result may reveal that you carry a BRCA1 and/or BRCA2 gene alteration for which the cancer risks have not been determined. It is common for African American individuals to receive this result following genetic testing. Overall, genetic testing for breast cancer risk has not been widely used by African Americans. Therefore, your test may reveal a change or alteration that has never been found before or has only been seen on rare occasions. In this instance, there most likely is not enough information available to understand the meaning of the variant. It is possible that the variant is a normal variation in the gene or it may indeed be associated with increased cancer risk. As research on the BRCA1 and BRCA2 genes continues the meaning of these variants are expected to be discovered. If you are found to have a genetic variant of uncertain significance your genetic counselor will contact you as soon as more information on this result becomes available..

## **Cancer Risks Associated with BRCA1 and BRCA2 Mutations**

Most research to learn of cancer risk in individuals with BRCA1 and BRCA2 mutations have included large families with many individuals affected with breast and ovarian cancer. More recent studies of families in the general population have found lower cancer risks in families that carry BRCA1 and BRCA2 mutations. Therefore, the cancer risk figures in individuals with BRCA1 and BRCA2 mutations are broad and may be revised as more research findings becomes available.

Keep in mind that very few African American families took part in studies to determine cancer risk for individuals who have a BRCA1 or BRCA2 mutation. However, it is thought that the risk of cancer in BRCA1 and BRCA2 African American families is similar to existing estimates, but at this time, there is no official data to support this. It is hoped that cancer risk information for hereditary African American families will be available in the future by recruiting willing individuals, such as yourself, into relevant research projects.

Overall, a woman with a BRCA1 or BRCA2 mutation is more likely to develop breast and/or ovarian cancer in her lifetime. However, having a mutation does not

guarantee that a woman will develop cancer. Therefore, having a mutation does not tell a woman whether she will develop cancer, what age the cancer might develop or, the type of cancer that might develop.

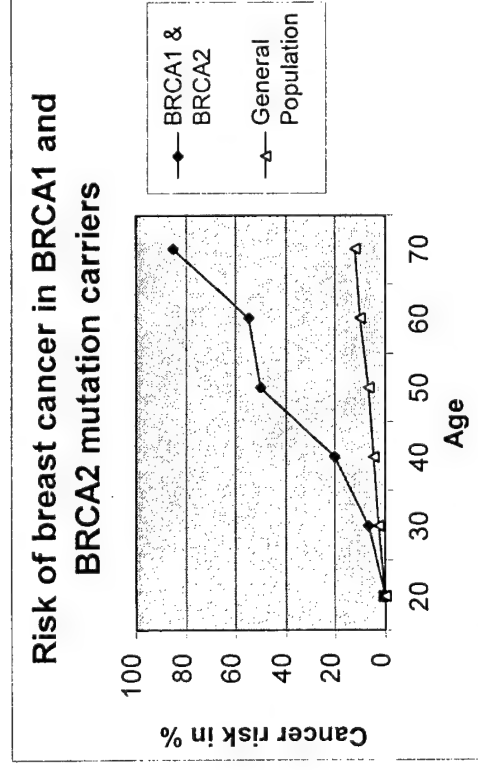
There are different cancer risks associated with carrying a BRCA1 or BRCA2 mutation depending on whether a woman has already had a cancer diagnosis. As mentioned, the following risk estimates have broad ranges and are based on estimates from different studies. In addition, these estimates can vary based on a woman's family history and her age.

A woman who has not been diagnosed with cancer:

- Has a lifetime risk of 55%-85% of developing breast cancer if she has a BRCA1 or BRCA2 mutation
- Has a 15%-60% lifetime risk of developing ovarian cancer with a BRCA1 mutation and a 15-25% chance of developing this cancer with a BRCA2 mutation

## Risk of other cancers with BRCA1 and BRCA2 mutations

- A woman with a BRCA1 or BRCA2 mutation may also have an increased risk for developing colon cancer
- There are slightly elevated risks for developing other rare cancers with a BRCA2 mutation including pancreatic, gallbladder, bile duct, stomach and skin (melanoma) cancers.
- These other cancers can also be found in male mutation carriers. In addition, males who have BRCA1 or BRCA2 mutations have an increased risk for developing prostate cancer. On rare occasions breast cancer can also develop in men who carry mutations in BRCA2 and possibly BRCA1 mutations.



### A woman who has had breast cancer:

- has up to a 65% risk of developing breast cancer in her unaffected breast with a BRCA1 mutation and up to 50% with a BRCA2 mutation
- has a possible increased risk of developing breast cancer again in the same breast (ex. following a lumpectomy) with mutations in both BRCA1 and BRCA2
- has a 30%-55% risk of developing ovarian cancer with a BRCA1 mutation and a 10%-25% risk of developing this cancer with a BRCA2 mutation

## Cancer Screening Recommendations

Although there are no proven ways to prevent cancer, early detection through screening increases treatment success. Cancer screening is most effective when it is done on a regular basis with repeat intervals determined by your physician. Knowing when is a good time to begin cancer screening, the frequency of the screening and which cancers you should be screened for are important for early detection of cancers. All of these factors depend on your personal health, your age, and your personal and family history of cancer. In addition to screening, careful monitoring for symptoms of cancer is also important.

The following are the most common screening techniques for cancers that are associated with an inherited susceptibility to breast cancer.

### Breast Cancer

*Mammogram*- An X-ray of the chest

*Clinical Breast Exam (CBE)* -A breast exam by a doctor or nurse using the pads of the fingers to feel for lumps or other changes.

*Breast Self-Exam (BSE)*- A personal examination of one's own breasts

### Ovarian Cancer

*Pelvic Exam*- Feeling of the uterus, vagina, ovaries, fallopian tubes, bladder and rectum by a physician to find any abnormality in their shape or size. A Pap test, a good test for cancer of the cervix, is often done along with pelvic exam, but it is not a reliable way to find or diagnose ovarian cancer

*Transvaginal ultrasound (TVS)*- Allows for the visualization of the ovaries on a screen by placing a probe in the vagina. Healthy tissues, fluid filled cysts, and tumors often look different on this picture.

*CA-125 blood test*- A test to measure the level of the protein *CA-125* in the blood which is often found in higher than normal amounts in the blood of women with ovarian cancer

### Colon Cancer

*Digital rectal exam (DRE)*- An exam in which the doctor inserts a lubricated, gloved finger into the rectum to feel for abnormal areas.

*Fecal Occult Blood Test(FOBT)*- A test to check for hidden (known as occult) blood in the stool.

Sometimes cancers or polyps can bleed, and *FOBT* is used to detect small amounts of bleeding.

*Sigmoidoscopy*- An examination of the rectum and lower colon with a lighted flexible, hollow tube which is about the thickness of a finger.

*Colonoscopy*- An examination of the rectum and the entire colon also performed with a lighted flexible.

hollow tube. A colonoscopy allows the doctor to see much farther into the colon than a sigmoidoscopy

The following table summarizes current screening recommendations. It is separated by recommendations for women in the general populations and for women who have a high risk for developing breast cancer. Bear in mind that your personal physician can help you make a decision about a screening regimen that is most appropriate for you.

Type of Cancer	General Population	BRCa mutation carriers and high risk women
Breast	<i>Mammograms</i> every 1 to 2 years starting at age 40, yearly after age 50. <i>CBE</i> every three years beginning at age 20 and yearly after age 40. Monthly <i>BSE</i> beginning at age 20	Annual <i>mammograms</i> beginning at age 25 to 35 years. <i>CBE</i> 2-4 times a year beginning at age 25 to 35 years. Monthly <i>BSE</i> beginning by age 18-20
Ovarian	No standard recommendation. Annual <i>pelvic examination</i> should begin at age 18 or when sexual activity begins along with a Pap test (to detect cervical cancer)	<i>Pelvic exams</i> along with <i>CA-125 blood test</i> and <i>TVS</i> yearly or twice a year beginning at age 25 to 35 years.
Colon	<i>FOBT</i> and <i>DRE</i> yearly beginning at age 50. <i>Sigmoidoscopy</i> should be performed every three to five years by age 50.	Generally the same for the general population but possible screening should begin at an earlier age. However, those with a family history should consider <i>colonoscopy</i> which is usually repeated less frequently than <i>sigmoidoscopy</i> .

## Breast and Ovarian Cancer Prevention

Women from high-risk breast and ovarian cancer families often wonder how they can prevent cancer or avoid developing another cancer. As previously mentioned, there are no proven ways to prevent cancer. However, in addition to screening to help find cancer early, there are choices you can make that may help to reduce your risk of getting cancer. Of course, you can consider these options without having genetic testing or if you test negative for mutations in BRCA1 or BRCA2.

### Prophylactic Surgery

*Prophylactic surgery* involves removing healthy breasts and/or ovaries in order to reduce the chances of developing cancer. Removal of healthy breast tissue (known as prophylactic mastectomy) can significantly reduce the risk of developing breast cancer in women at high risk, including women with a BRCA1 or BRCA2 mutation. However, because this surgery cannot remove all breast tissue, there is still a small chance that a woman will develop breast cancer after having a prophylactic mastectomy.

Removing the ovaries to prevent ovarian cancer is known as a prophylactic oophorectomy. This surgery significantly reduces the risk for ovarian cancer. However, there is still a small chance of developing an ovarian-like cancer in the lining of the abdominal cavity (known as primary peritoneal carcinoma) after the ovaries are removed.

In addition to reducing ovarian cancer risk, a recent study has found that prophylactic oophorectomy reduces the risk of breast cancer in women with a BRCA1 or a BRCA2 mutation. It appears that the amount of risk reduction is most significant in women who had their ovaries removed before age 40. However, women who had their ovaries removed before age 50 also benefited. Nonetheless, bear in mind that the main reason to consider prophylactic oophorectomy is to reduce ovarian cancer risk.

### Chemoprevention

Listed below are medications that can be taken to reduce breast and ovarian cancer risk (known as *chemoprevention*).

*Tamoxifen*- Tamoxifen is a hormonal medication that is commonly used as a treatment for women with breast cancer to prevent a recurrence and reduce the chance of developing another breast cancer. Tamoxifen has also recently been found to reduce the risk of developing breast cancer in women at increased risk (who have not had a breast cancer diagnosis). In addition, tamoxifen has been found to reduce the risk of developing a second breast cancer in patients with a BRCA1 and BRCA2 mutation. It is hoped that use of this medication will also reduce the risk of breast cancer in women with a BRCA1 or BRCA2 who have never had the disease.

*Birth Control Pills*- There is evidence that women with a BRCA1 or BRCA2 mutation who used birth control pills for an extended period of time significantly reduced their risk of ovarian cancer. Women with a family history of ovarian cancer who are not found to carry a mutation in BRCA1 or BRCA2 may also benefit from using birth control pills. It is important to mention that in addition to birth control pills, anything that keeps a woman from ovulating every month significantly reduces the risk of ovarian cancer, including pregnancy and breast feeding.

### Tubal Ligation

Studies of women in the general population have found that *tubal ligation* (having one's fallopian tubes tied to prevent pregnancy) can significantly reduce the risk of ovarian cancer. There is also recent preliminary evidence that suggests that tubal ligation reduces the risk of ovarian cancer in women with a BRCA1 or BRCA2 mutation.

### Lifestyle Factors

Certain behaviors are believed to decrease cancer risk, such as limiting alcohol consumption and increasing regular exercise. Research results on the benefits of these behaviors are based on studies in the general population and the effects of these behaviors in BRCA1 and BRCA2 mutation carriers are unknown.

It is important to mention that what we now know about cancer is due in large part to research. Your participation in this study will help us to learn more about hereditary breast cancer in African American women. In addition, by taking part in other studies in the future, you could help researchers find better ways of preventing and treating cancer.

## GLOSSARY

*Atypical hyperplasia:* A non-cancerous condition in which breast tissue has certain abnormal features. Women with this condition have an increased risk of breast cancer.

*Benign:* Not cancerous; does not invade nearby tissue or spread to other parts of the body.

*Biopsy:* The removal of a sample of tissue, which is then examined under a microscope. Excisional biopsy is surgery to remove an entire lump and an area of normal tissue around it. In incisional biopsy, the surgeon removes just part of the lump. Removal of tissue with a needle is called a needle biopsy.

*Carcinoma:* Cancer that begins in the lining or covering of an organ.

*Chemoprevention:* The use of medications to reduce the risk of developing cancer

*Ductal Carcinoma in-situ (DCIS):* Abnormal cells that involve only the lining of a duct and have not spread outside the duct to other tissues in the breast. Also called intraductal carcinoma.

*Estrogen:* A female hormone

*Gene:* The basic unit of heredity passed from parent to offspring. Genes are pieces of DNA, and most genes contain the information for making a specific protein.

*Hereditary:* Genetically transmitted from parent to child.

*Inherited:* Transmitted through genes from parents to offspring.

*Lobular carcinoma in-situ (LCIS):* Abnormal cells in the lobules of the breast. This condition seldom becomes invasive cancer, however having this condition is a sign that a woman has an increased risk of developing breast cancer.

*Lumpectomy:* Surgery to remove only the cancerous breast lump; usually followed by radiation therapy.

*Mastectomy:* Surgery to remove the breast (or as much of the breast as possible).

*Mutation:* A change in a gene which may result in a specific disorder.

*Oophorectomy:* Surgery to remove the ovaries.

*Ovaries:* The pair of female reproductive organs that produce eggs and hormones.

*Pathology:* Identification of diseases by studying cells and tissues under a microscope.

*Predisposition:* To have the tendency to develop a disease in the future.

*Progesterone:* A female hormone.

*Prophylactic surgery:* Removal of healthy at-risk tissue to prevent the development of cancer.

*Screening:* Checking for disease when there are no symptoms.

*Sequencing:* The process of determining the order of base sequences in a gene.

*Sporadic-* In medical terms refers to a disease that occurs rarely, without regularity, and with no known specific cause.

*Susceptibility:* To have the tendency to develop a disease in the future.

*X-Ray:* High-energy radiation. It is used in low doses to diagnose diseases and in high doses to treat cancer.